

# **REGEN THERAPEUTICS PLC**

## **DECEMBER CITY PRESENTATION**

[www.regentherapeutics.com](http://www.regentherapeutics.com)

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## **Forward Looking Statements**

**This document and the presentation to which it relates includes forward-looking statements that relate to ReGen's objectives, estimates and goals. Any statements that are not statements of historical fact should be considered forward-looking statements. The company's business is subject to numerous risks and uncertainties, including the necessity to conduct further clinical trials and related studies (such as toxicity and bio-equivalence), the ability to develop and manage a scaleable manufacturing process for Colostrinin™, product testing and regulatory approval, efficacy and safety of Colostrinin™'s constituent peptides in the treatment of any disease or condition in both the Colostrinin™ peptides and zolpidem, the completion of certain acquisitions and the ability to successfully integrate acquisition targets. These and other risks and uncertainties could cause ReGen's actual results and developments to be materially different from those expressed or implied by any of these forward-looking statements.**

**Key assumptions made in preparing this document and the presentation to which it relates include:**

- We do not expect sales of Colostrinin™ as a nutraceutical before 2006.**
- The Company has a pre clinical programme to develop the potential of Colostrinin™ peptides as a treatment for Alzheimer's disease and other CNS illnesses.**
- It is unlikely that we will receive a milestone payment for Colostrinin™ constituent peptides as a treatment for Alzheimer's disease, or other CNS illnesses before 2007.**
- No payments for zolpidem before 2007.**



# REGEN THERAPEUTICS PLC

Presentation by:

Percy Lomax

Chairman and Chief Executive



# THE COMPANY

- ReGen Therapeutics Plc was founded in 1998 to acquire IP related to Alzheimer's disease.
- Floated on Ofex December 1998.
- AIM flotation March 2000.
- Capital raised so far £15m.
- Acquired Guildford Clinical Pharmacology Unit Limited (GCPUL) October 2004.
- ADR programme established 4<sup>th</sup> December 2004, quotation March 2005.
- Option to acquire Sciencom Limited entered into – potential new use of zolpidem for treatment of secondary effects of stroke and other brain injury.



# OUR BUSINESS

ReGen Therapeutics Plc has three business lines:

- Pharmaceutical drug development,
- Human and Veterinary nutraceutical products,
- Clinical Research Organization.



# PHARMACEUTICAL DRUG DEVELOPMENT

- Scientific and clinical data on Colostrinin™ has shown potential as a treatment for Alzheimer's disease.
- Colostrinin™ itself is complex (not itself a classical drug candidate) and consists of low molecular weight peptides, generally known as proline-rich polypeptides.
- Therefore programme now running to develop a pharmaceutical ingredient based on Colostrinin™ constituent peptides.
- Classical pharmaceutical pre-clinical candidate possible by 2007.
- Zolpidem – clinical studies for use in secondary effects of stroke and other brain injuries.



# COLOSTRININ™

- Proline-rich polypeptide complex derived from colostrum.
- Colostrum is a mammal's first milk after the birth of an offspring.
- Patented in USA, UK, Australia, New Zealand, South Africa, China, Turkey, Israel, Russia and South Korea - patents pending in Europe and other major countries.
- Clinically tested in over 150 human subjects.

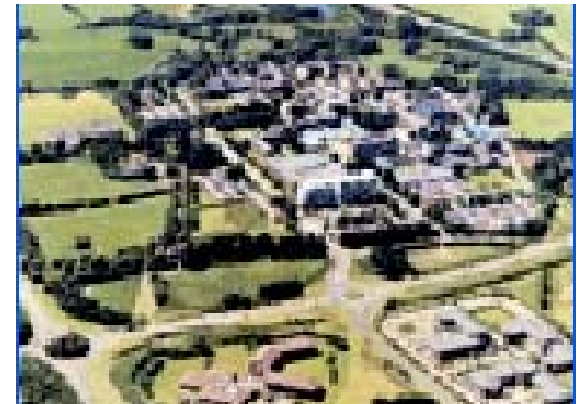
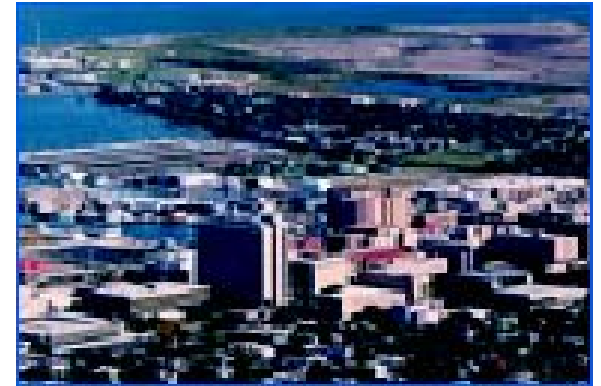




# RESEARCH

Science programmes at:

- University of Texas Medical Branch, Galveston, Texas, USA.
- Roswell Park Cancer Institute, Buffalo, NY, USA.
- Open University – UK.
- St. George's Hospital, Tooting – UK.



# IN-VITRO RESEARCH

- ***Journal of Molecular Neuroscience, January 2003:*** Colostrinin™ shown to reduce intracellular oxidative metabolism which is central to cell proliferation, differentiation and apoptosis.
- ***Neuropeptides, July 2005:*** Colostrinin™ shown to prevent the aggregation of  $\beta$ -amyloid peptide A $\beta$  (1-40) and its toxic effect on neuronal cells
- ***Cellular and Molecular Neurobiology, November 2005:*** Colostrinin™ shown to block the proliferation and promote the differentiation of primary cells into neuronal cells.
- ***Unpublished, April 2005:*** Colostrinin™ and a Colostrinin-derived synthetic nonapeptide (NP pol) shown to protect dopaminergic cells from toxic insult.
- ***21<sup>st</sup> International Conference of Alzheimer's Disease International, October 2005:*** Colostrinin™ shown to increase lifespan of senescence accelerated mouse cells and normalise mitochondrial function. ***Submitted for publication in Neuropeptides.***



# IN-VIVO RESEARCH

- ***Pharmacology, Biochemistry and Behaviour, June 1999:***  
Colostrinin™ was shown to facilitate learning and memory in old rats in a Morris Water Maze study
- ***Behavioural Brain Research, Jan 2001:***  
A Colostrinin-derived synthetic nonapeptide (NP lis) was shown to delay the extinction of long-term memory in old rats in a Morris water Maze study
- ***Federation of European Neurological Societies, July 2004:***  
Colostrinin™ was shown to have a very strong effect in enhancing memory when compared with controlled saline injections in young chicks.
- ***Society for Neuroscience, October 2004:***  
Colostrinin™ was shown to reduce memory impairment induced by beta-amyloid, a toxic protein involved in Alzheimer's in young chicks



# CLINICAL RESEARCH ON ALZHEIMER'S

- *Medical Science Monitor*, A long term study – extension of a double blind placebo controlled study, 2002:  
Scientists found: Colostrinin™ “is a very promising preparation” which can be used to “inhibit” or “retard” the development of Alzheimer’s disease.
- *Journal of Alzheimer’s Disease*, 2004:  
30-week trial of mild to moderate Alzheimer’s disease treatment  
Evidence of early beneficial effects on cognitive symptoms and daily functions.  
Statistically significant difference: ADAS-cog ( $p=0.02$ ) and IADL ( $p=0.02$ ).

# CLINICAL RESEARCH ON ALZHEIMER'S - SUMMARY

- *Safety:*

No adverse side effects or safety issues arose from the 30 week trial in 106 Alzheimer's disease sufferers.

12m db placebo/selenium-controlled, 45 subjects/15 on Colostrinin™ (13 up to 28 months) no side effects/safety issues

Three other trials have shown no adverse side effects/safety issues.

- *Efficacy:*

Efficacy demonstrated in mild and moderate cases; with greater efficacy seen in earlier-stage patients.



# ALZHEIMER'S DISEASE

- Alzheimer's disease is a silent epidemic of dementia that is occurring in societies with ageing populations.
- Alzheimer's drug sales \$3.2bn end 2004. Trebled since the year 2000.\*
- Nutraceutical would address part of \$140 billion global nutraceutical market.\*\*

\* IMS Health

\*\* Nutritional Business Journal



# PEPTIDE MIMETIC DEVELOPMENT PROGRAMME

- Programme underway to develop peptide mimetics for Alzheimer's disease, where we have evidence of Colostrinin™ clinical activity and safety.
- Based on research evidence Colostrinin™ and constituent peptides may have efficacy in treatment of many age-related disorders including neurodegenerative diseases such as:
  - Parkinson's Disease – initial data from in-vitro study suggests that Colostrinin™ and peptides within it may protect dopaminergic neurones against degeneration.
  - Multiple Sclerosis.
  - Amyotrophic Lateral Sclerosis.



# ZOLPIDEM

- Widely prescribed drug – thus characteristics known.
- “Open” clinical case observations have shown zolpidem can normalise brain dormancy secondary to a primary brain lesion.
- Brain dormancy secondary to stroke, traumatic brain injury, vascular dementia and Bells palsy have shown response.
- Estimated market size \$4.3bn\*.
- Clinical trial expected to start during 2006.

\* ReGen estimates based on publicly available US government data.



# PHARMACEUTICAL LICENSING STRATEGY

- Initially to develop a classical pharmaceutical based on active principle within Colostrinin™ to pre-clinical or Phase I.
- To develop a new use for zolpidem through Phase II.
- Pre clinical and Phase I deals have attracted upfront monies of \$20m in 2004, total deal value \$77m\*.

\* Source Windhover In-Vivo



# NUTRACEUTICAL COLOSTRININ™

- Colostrinin™ has originally been developed as a pharmaceutical product, thus there is more clinical and *in-vitro* data than normally required for nutraceutical applications.
- Licensing revenues from a nutraceutical product are currently expected during 2006.
- ReGen appointed licensing specialist has generated extensive enquiries from co-development partners – discussions are ongoing.
- Veterinary trial planned quarter 1 2006.



# NUTRACEUTICAL MARKET (HUMAN)

US industry reference *Nutritional Business Journal*  
(2000) estimated:

- Global market to be US \$140bn, equal to half of global pharmaceuticals market.
- The US market accounts for 35% of the worldwide market.
- European market is of a similar size to the US.
- Japan and Asia are increasingly important markets.



# **MANUFACTURE US BOVINE COLOSTRUM**

- Industrial scale process defined at US bovine colostrum company.
- US by far the largest single market.
- Know-how/facilities and equipment.
- Collection/pooling/standardised raw material.
- Cost/time-effective production of nutraceutical grade material.



# CONTRACT RESEARCH

- GCPUL is revenue generating.
- Wide ranging Phase I and Phase II expertise.
- Capable of significant expansion.
- Experienced management.



# SUMMARY

- Drug development:
  - Colostrinin™ peptide mimetic programme underway.
  - One synthetic peptide (NP lis) has shown improved memory/ cognitive function in rats.
  - Another synthetic peptide (NP pol) has shown protection of cells from toxic insult in a model predictive of potential activity in Parkinson's disease.
  - Zolpidem to enter clinical trials in 2006.
- Colostrinin™ nutraceutical development:
  - Discussions with co-development/commercialisation partners ongoing. Revenues expected Quarter 4 2006.
  - Industrial scale process defined.
- Further acquisition targets identified.
- ADR programme established December 2004 and quoted March 2005.

# THE OPPORTUNITY

- ReGen now anticipates profitability in 2007.
- News flow over next year is anticipated to show a nutraceutical deal and nutraceutical sales.
- There could be further positive news on Colostrinin™ peptides and zolpidem.
- Further acquisition targets identified to build business.



A New Use for a well-known drug:

# **ZOLPIDEM**

A major role in rehabilitation after stroke  
and other brain injuries





# INTRODUCTION

- ZOLPIDEM – S African TV article



# THE PROPOSITION

- The reversal of brain ‘dormancy’ at sites removed from a primary site of brain damage (e.g. stroke, head trauma, viral infection, near-drowning).
- Leading to improvement of those functions controlled by the ‘dormant’ brain areas.



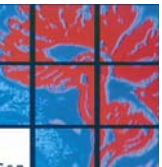
# THE OPPORTUNITY

- Significant, independently validated effect in 80+ cases with Zolpidem a well-known, soon to be off patent drug.
- Usefulness of existing/generic ('high dose' tablets) limited by sedation, slow/variable absorption.
- New 'low dose' tailored formulations required:
  - Diagnosis/top-up
  - Maintenance
- New use patents pending/formulation patents possible.
- Totally unmet need in large diverse population.



# STRIKING IMPROVEMENTS IN QUALITY OF LIFE IN 80+ PATIENTS

- Aphasia (speech cognition).
- Dysarthria (word articulation).
- General cognition and IQ.
- Ataxia (limb coordination/posture).
- Hearing.
- Basic reflexes (swallowing and continence).



# NEW FORMULATIONS

- Maintenance:
  - Nasal/sublingual
  - patch
  - oral controlled release
- Identification of responder/top-up dosing:
  - Nasal/sublingual

# US PATIENT DATA

<b>Condition</b>	<b>USA prevalence (millions)</b>
<b>Traumatic Brain Injury:</b>	
<b>major</b>	<b>0.54</b>
<b>minor</b>	<b>5.3</b>
<b>Stroke</b>	<b>4.8</b>
<b>Vascular dementia</b>	<b>1.5</b>
<b>Millions of patients in USA</b>	<b>12.14</b>

Source: JAMA 285: 594 (2001); Stroke(1996)  
Mar;27(3):370-2.

# POTENTIAL WORLD MARKET SIZE

- Potential World market for our new use of zolpidem is \$4.3 billion. Based on:
  - Known US patient data
  - Assuming US accounts for about half of world market
  - Assuming 50% of patients respond
  - Price per treatment \$1 per day

# REGEN PLANS

- Perform ‘clinical proof of concept study’ with new formulation to show that it at least matches 5mg tablet in terms of ‘anti-dormancy’ effect but with less sedation.
- Target and discuss potential collaboration with formulation and commercialisation partners.

